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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	PAPER NUMBER
1652	//

DATE MAILED: 03/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,126	HAN ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *9,12-45,49-58,65 and 66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11,46-48 and 59-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed February 14, 2002 (Paper No. 10) amending claims 1-3 and 59 has been entered.

Claims 1-66 are pending.

Election/Restriction

Claims 9, 12-45, 49-58, 65 and 66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups II-XVIII, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Applicant's election without traverse of Group I, claims 1-8, 10, 11, 46-48 and 59-64, in Paper No. 10, page 5, is acknowledged.

Claims 1-8, 10, 11, 46-48 and 59-64 are under consideration.

Information Disclosure Statement

The instant application contains no IDS.

Specification

The specification is objected to because of the following: it refers to the same position as "1508" and "1568" on page 96, line 33, and page 97, line 12, respectively. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 11, 46-48 and 59-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a nucleotide sequence that hybridizes under moderately or highly stringent conditions to a nucleotide sequence encoding SEQ ID NO:2 or the specific nucleotide sequence of SEQ ID NO: 1. The hybridization conditions are not specified rendering the limitations on the structure not sufficiently described. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of claim 1, including partial DNA sequences and DNAs encoding inactive variants of SEQ ID NO:2. The specification discloses only a single species of the claimed genus, SEQ ID NO: 1. Moreover, the specification fails to describe any other representative species by

common identifying characteristics and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Claim 2 is drawn to a DNA that hybridizes under moderately or highly stringent conditions to a) a nucleotide sequence that encodes a polypeptide having at least 70% identity to SEQ ID NO: 2 and retaining an unspecified activity of SEQ ID NO:2; b) a DNA encoding an allelic or splice variants without specific activity or c) a DNA comprising a fragment encoding at least 25 amino acids and retaining an unspecified activity of SEQ ID NO:2. In addition to the lack of written description of a generic embodiment as applied to claim 1 above, claim 2 comprises the generic embodiments of DNAs of a), b) and c), *supra*. Therefore, the claim encompasses a diverse genera of molecules of different structures and functions including inactive variants thereof. With regard to a) and c), the specification fails to provide any structure: any specific function correlation present in all members of the claimed genus. With regard to b), the specification discloses only one splice variant within the scope of the genus: SEQ ID NO:1. It discloses one SNP (pages 96-97, Example 9; SEQ ID NO:18). There is no description of other mutational sites for allelic variants or exon/intron splice junction for splice variants that exists in nature, and there is no description of how the structure of SEQ ID NO: 1 or SEQ ID NO:18 relates to the structure of other allelic or any splice

variant. Allelic or splice variants are variant structures, and in the present state of the art the structure of one or two does not provide guidance to the structure of others. The common attributes of the genus are not described. One of skill on the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of the genus is not representative of the variants of the genus and is insufficient to support the claim.

Claim 3 is drawn to a DNA that hybridizes under moderately or highly stringent conditions to a nucleotide sequence that encodes a polypeptide having at least one substitution, insertion or deletion in SEQ ID NO:2 and retains an unspecified activity of SEQ ID NO:2. The claim does not place any limit on the number of amino acid substitutions, insertions and deletions that may be made to SEQ ID NO:2. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between the genus members is permitted. No common structural attributes identify the members of the genus to allow to distinguish compounds in the genus from others in the protein class. Therefore, SEQ ID NO:1 alone is insufficient to describe the genus.

Claim 59 is drawn to a diagnostic reagent comprising a DNA encoding a fragment, variant or homolog thereof including allelic and spliced variants thereof. There is no limitations on either the structure or function of an encoded protein. This genus includes many structurally and functionally unrelated proteins. For the reasons

discussed above, a single member of the genus, SEQ ID NO:1, alone is insufficient to describe the genus.

Claims 4-8, 10, 11, 46-48 and 60-64 are drawn to vectors, host cells and methods of use of the above DNAs and are included in the rejection as comprising the product lacking sufficient written description.

For the reasons discussed above, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-8, 10, 11, 46-48, 59-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding SEQ ID NO:1, does not reasonably provide enablement for a nucleotide comprising a nucleotide encoding a fragment of SEQ ID NO: 2 and having no specified function and various variants thereof of unknown structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification does not reasonably provide enablement for a DNA encoding a polypeptide comprising a fragment of SEQ ID NO:2 of at least 25 amino acids and retaining any of the activities of SEQ ID NO:2 or a variant of any structure retaining or

not retaining any of the activities of SEQ ID NO:2. The size and composition of said fragment are not limited.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any sequence that comprises a fragment of SEQ ID NO:2 or hybridizes thereto and encodes a polypeptide retaining its activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; © a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptide structure having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Furthermore, claims 1 and 59 encompass a DNA encoding a polypeptide retaining an activity and an inactive variant thereof. The specification does not teach how to use said inactive variant. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The state of the art does not allow the predictability of the properties based on the structure. The properties of a polypeptide of an unknown length and structure are unpredictable based on a fragment. Therefore, one skilled in the art would require guidance as to how to make a DNA encoding a polypeptide that has unknown, if any, homology to SEQ ID NO: 2 and retains its activity. Further, one skilled in the art would require guidance as to how to use a DNA encoding a polypeptide of unknown function comprising a fragment or variant of SEQ ID NO:2 and a DNA that hybridizes to SEQ ID NO:1 and encodes a sequence that has no known function in a manner reasonably

correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10, 11, 46-48 and 59-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "activity" without defining the specific function. A polypeptide may exhibit various different functions such as catalytic, regulatory, immunogenic, etc. Fragments/variants possessing any of these functions are not necessarily the same. Therefore, without pointing out the function there is no way of knowing what are the metes and bounds of the claims.

The claims recite "moderately or highly stringent [hybridization] conditions". Without knowing the exact conditions that can be defined differently in different experiments there is no way of knowing what are the metes and bounds of the claims.

Claim 2(b) recites "a nucleotide sequence encoding an allelic or splice variant of the nucleotide sequence as set forth in SEQ ID NO:1". It is confusing as drawn to a nucleotide sequence encoding a variant of a nucleotide sequence.

Claim 60 refers to claim 58 where it appears claim 59 is intended.

Claims 61-64 are confusing as using "a diagnostic reagent" for not diagnosing anything. Amending the claims to recite "reagent" would obviate this rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 59-64 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 59 and 60 are drawn to a diagnostic reagent comprising a DNA encoding SEQ ID NO: 2. This implies that said reagent is used for diagnostic of a specific disease or condition. Neither the specification nor the art of record disclose any disease or conditions that can be diagnosed with SEQ ID NO:1. The specification teaches that the expression of huE3α1 (SEQ ID NO:1) corresponds to a cachexia state with severe muscle wasting (pages 99-104, Examples 11 and 12). However, the muscle wasting at this stage of cancer is diagnosed visually and expression of many other proteins is changed. The finding of the aberrant expression of huE3α1 does not allow to predict the onset of any disease such as caner, for example, or any condition such as cachexia, for example, wherein they are not diagnosed otherwise before. The

measurement of the expression of huE3α1 does not allow to diagnose any disease or condition not *a priori* diagnosed by an independent method such as by the weighing of muscles in case of cachexia, for example. Therefore, diagnosing of an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a disease or condition that can be diagnosed by a diagnostic reagent comprising SEQ ID NO:1 or any variant or fragment thereof.

Claims 59-64 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention (see above).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10, 11, 46-48 and 59-64 are rejected under 35 U.S.C. 102(a) as being anticipated by Hillier et al.

Hillier et al. teach an EST of 682 bp that is 99.3% identical to SEQ ID NO:1 (EST Accession AI929033). Said EST comprises a fragment, a variant, an allele of SEQ ID NO:1 and will hybridize thereto under moderate or highly stringent conditions.

Claims 1-8, 10, 11, 46-48 and 59-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg et al.

Strausberg et al. teach an EST of 641 bp that is 99.5% identical to SEQ ID NO:1 (EST Accession AI361043). Said EST comprises a fragment, a variant, an allele of SEQ ID NO:1 and will hybridize thereto under moderate or highly stringent conditions.

Claims 1-8, 10, 11, 46-48 and 59-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Varshavsky et al.

Varshavsky et al. (US Patent 5,861,312) teach a murine UBR1 (SEQ ID NO:1) that is 86 % identical to SEQ ID NO:1 of the instant invention. As such, it comprises a fragment, a variant, an allele of SEQ ID NO:1 and will hybridize thereto under moderate or highly stringent conditions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

March 11, 2002